CHEM 2P21 Information Exercise Winter 2024

The objective of this exercise is to explore the scholarly biomedical, chemistry, green and patent literature. This exercise involves searching the chemistry literature in different ways looking for information, articles and patents using unique chemistry- and open-oriented databases. Note the Brock Library Chemistry and Biochemistry Library Research Guides for assistance.

Select **one** antifungal or antibiotic drug from these sites or one listed below for this assignment: Antifungal (Wikipedia), What are the most common antibiotics? (healthline), Azithromycin, Cephalexin, Ciprofloxacin, Clindamycin, Clarithromycin, Doxycycline, Levofloxacin, Meropenem, Metronidazole, Sulfamethoxazole, or Tobramycin.

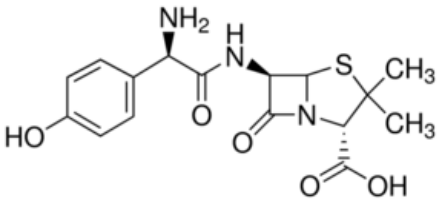
Consider learning more about your drug/chemical using a variety of chemistry databases and catalogs including: ChEMBL, ChEBI, ChemID Plus (NIH), DrugBank, Drugs.com, NCBI Chemicals & Bioassays (NIH), fisherscientific, Sigma-Aldrich, and RxList.

Use Zotero or zoterobib to create citations using American Chemical Society style. The ACS Guide to Scholarly Communication is an ACS publication that is constantly updated and provides access to the ACS Quick Style Guide that includes excellent information on writing, scholarship and style.

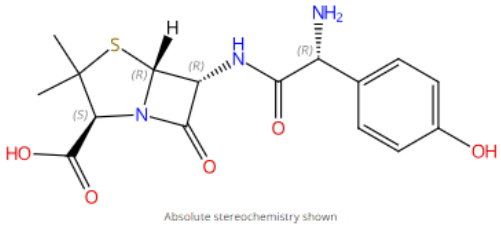
1. Complete the following for your small chemical / antibiotic / drug of choice using SciFinder-n:

   Chemical / Drug name: **Amoxicillin**
   Molecular Formula: **C16 H19 N3 O5 S**
   CAS Registry Number: **26787-78-0**
   IUPAC Name: **(2S,5R,6R)-6-[[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid**

   Insert one interesting image of your drug's chemical structure and name the source. **Here are two:**



Sigma-Aldrich



ACS SciFinder-n

2. Comment on this drug's cost and availability using a commercial supplier e.g. Sigma-Aldrich, Chemical Book, or use the SciFinder-n "Commercial Sources" tab, and comment whether it would be cheaper/easier to make the drug or purchase it yourself? Explain why.

Depending upon how amoxicillin is formulated as a pharmaceutical drug it costs approximately $60-$75/gram or $16/5ml suspension 100ml bottle. Noting the aromatic rings, substitution and stereochemistry, it would be difficult to formulate and is just too cheap not to buy in bulk.

3. In one or two sentences explain why this chemical/drug is important summarizing its bioactivity, chemical drug classification, bioactivity, target indicator, mode of action and how it works as an antibiotic/antibacterial drug.

   Amoxicillin is one of the most popular beta-lactam antibiotics used to treat bacterial infections mainly in children. As a small molecule penicillin organoheterocyclic conjugate acid, Amoxicillin binds to, weakens and causes cell lysis, inactivating penicillin-binding proteins (PBPs) located in bacterial cell walls in both negative- and gram- positive bacteria.

4. Go to the SciFinder-n database. You need a register for a new or remember your personal SciFinder-n account username/password. Complete the following:

   How many retrieved ***reactions*** searching your drug as a *product*? **189**
   How many retrieved ***reactions*** searching your drug as a drawn structure? **95**
   How many retrieved Results when searching your drug name and the keyword prepar* in Reference titles? **492**
   How many of these references are patents? Document Type = Patent? **317**

   Sort citations by relevance, yield, number of steps, date, relevance… Select the most recent or one of the most interesting patents, check out the citation, indexing, click on PatentPak and Full Text, and cite it below using ACS Citation (with title) style:

   Leenderts, E J A. Preparation of beta-lactam antibiotics in the presence of urea or amide. EP 0953569A1, Nov 3, 1999.

5. Go to PubChem, find your drug, check out all contents, completing the following:

   What is the PubChem CID for your drug? **33613**
   What is the next highest MeSH and Thesaurus Tree classification names for your drug? **Amoxicillin is a type of Ampicillin and Penicillin Antibiotic.**

6. Go to the Reaxys database (no registration needed). Do a "Quick search" which is the default setting. Search for your drug, view the most appropriate entry, indicate:

   What is the Reaxys ID number for your drug? **4274654**
   Number of Reaxys preparations **23,** documents **27,230**, and reactions **228.**
   Click on the Retrosynthesis tab at the top of the Reaxys search page, look up your compound and run your synthesis which takes all reactions, variant compounds and then looks to produce an algorithmically AI search reaction tree complete with experimental procedures when available for your benefit. View the future of synthetic organic chemistry that will soon AI data to run biological sequences, target groups, steps, reactions… all linked to article and patent citations.
   How many published retrosynthesis did Reaxys find? **Five**

7. Using Reaxys, click on new search, do a "Query builder" search this time which guides you through a search strategy one step at a time. Search for your drug (e.g. CAS no.), select "Search in: Reactions", filter/limit to "Yield", filter/limit to Document Type "article", sort by "Reaxys ranks" and pick one of the current or most interesting articles. What is this reaction yield **76%** and include the citation using ACS Citation (with title) style.

Kuprienko, O. S.; Serchenya, T. S.; Vashkevich, I. I.; Harbachova, I. V.; Zilberman, A. I.; Sviridov, O. V. Conjugates of Aminopenicillins with Proteins: Synthesis, Immunogenic Properties, and Binding to the β-Lactam Receptor and Antibodies. Russ J Bioorg Chem **2022**, 48 (1), 105–114. https://doi.org/10.1134/S106816202201006X

8. Using Reaxys, click on "Quick search", type in your patent citation used in question number 4, find the Reaxys citation, click on Full Text, which takes you to the Espacenet database. This is an amazing European Union open patent database. How many claims for this patent? **17**

   In one or two sentences what is novel or unique about this patent and these claim(s)?

   This patent claims a new method for the preparation of beta-lactam antibiotic compounds including Amoxicillin based on previous patents and research. This new method uses acid derivatives, salts, and processes in the presence of urea or amide derivatives that provides unique formulations and experimental conditions.

9. You've been hired by an international pharmaceutical company as a researcher / chemist / scientist and challenged to respond to the CDC's 2019 AR Threats Report. Read the entire document! Using your favorite scholarly database, find a recent scholarly peer-reviewed experimental biochemistry, biological, pharmacology, biomedical, or chemistry journal article **using one of the 18 antibiotic-resistant bacteria or fungi** that speaks to this threat. This article has to include experimental methodology and data to answer question 10. Cite the database used, your organism's scientific name, and the article found using ACS Citation (with title):

   Selected Web of Science Core Collection database, Shigella,

   Dhara, D.; Mulard, L. A. Exploratory N-Protecting Group Manipulation for the Total Synthesis of Zwitterionic *Shigella Sonnei* Oligosaccharides. *Chem. Eur. J.* **2021**, chem.202003480. DOI:10.1002/chem.202003480.

10. In one or two sentences, use your own words to comment on whether the paper you picked for Question number 9's methodology, reactions, data, and techniques are (or are not) indicative of the 12 Principles of Green Chemistry.

    I am speaking to "Safer Solvents and Auxiliaries" and this paper researchers' use of solvents. No comments were found in the methodology or results that spoke to the selection, use, toxicity, fewest life cycle environmental impact or the safe disposal of glycoside derivatives or end product Acet/H2O, DCA-Cl, Et3N, CAN, MeOH, THF… solvents.

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